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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,793	02/27/2001	Hiromasa Miyaji	766.46	3687

5514 7590 03/20/2007  
FITZPATRICK CELLA HARPER & SCINTO  
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EXAMINER

SHAHER, SHULAMITH H

ART UNIT	PAPER NUMBER
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1647

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/20/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

## Office Action Summary

Application No.

09/763,793

Applicant(s)

MIYAJI ET AL.

Examiner

Shulamith H. Shafer, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 03 January 2007.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-48 is/are pending in the application.
- 4a) Of the above claim(s) 13-28, 30-41 and 43-45 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-13, 29, 42 and 46-48 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☒ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 5/10/01, 4/9/02.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_.

### **Detailed Action**

#### ***Status of Application, Amendments, And/Or Claims:***

#### ***Restriction Requirement:***

Applicants' election, of Group I, Claims 1-12, 26-29, 42 and 46-48 drawn to a polypeptide and a DNA sequence encoding said polypeptide, in the reply filed on 3 January 2007 in response to Office Action of 5 December 2006 is acknowledged. In response to requirement for species election, applicants have elected DNA of SEQ ID NO:2 encoding polypeptide of SEQ ID NO:1 (in response to Species election 1) and side effects of chemotherapy (in response to Species election 5). Because Applicants did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-48 are pending in the instant application. Claims 13-28, 30-41, and 43-45 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 1-12, 29, 42, and 46-48 are under consideration to the extent they read on the elected invention.

#### ***Priority:***

Acknowledgment is made of applicants' claim for foreign priority based on an application filed in Japan on 27 of August 1998. It is noted, however, that applicant has not filed a certified copy, of the Japan 10/241248 application as required by 35 U.S.C. 119(b). Therefore, benefit of the foreign priority filing dates is not granted. Benefit is granted to the date of PCT/JP99/04602, 26 of August 1999.

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***Information Disclosure Statement:***

The information disclosure statement (IDS) filed 10 May 2001 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because reference 10 does not disclose a publication date; the reference has therefore been lined through and not considered.

The information disclosure statement filed 9 April 2002 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because references 1-4 list Accession Numbers without identifying the appropriate databases. Furthermore, references 5-9 are duplicates of references cited on IDS submitted 10 May 2001. The references have therefore been lined through and not considered.

Applicants are advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

**Objections**

***Title:***

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The word "novel" should be omitted from the title, since all patents contain novel subject matter. The claims are drawn to polypeptides which have nucleoside transporting activity and polynucleotides encoding said polypeptides.

The following title is suggested: "Nucleoside transporter polypeptides and polynucleotides encoding the polypeptides".

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**Specification:**

The disclosure is objected to because of the following informalities: The specification identifies two sections labeled (3): the first starting on page 36 and the second beginning on page 39 (2<sup>nd</sup> sentence from the bottom). Appropriate correction is required.

**Claims:**

Claims 1-12, 42, and 46-48 are objected to as encompassing non-elected inventions. Appropriate correction is required.

**Rejections**

**35 U.S.C. § 101**

35 U.S.C. § 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4, and 46 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 1 and 2 are directed to a polypeptide; claims 3, 4 and 46 recite DNA encoding a polypeptide. The claims as written do not sufficiently distinguish over a polypeptide or gene coding a polypeptide that naturally exists in cells because the claims do not particularly point out any non-naturally occurring differences between the claimed sequences and naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. (See *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g. by insertion of language indicating an isolated polypeptide and or isolated DNA (See MPEP 2105).

**35 U.S.C. §§ 101 and 112, First Paragraph:**

The text of 35 U.S.C. § 101 is set forth above.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim(s) 1-12, 29, 42 and 46-48 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, substantial or specific asserted utility or a well established utility.

When determining whether an applicant has described the utility of invention, one has to determine whether the applicant has described a well-established utility. If not, has the application made any assertion of specific, substantial and credible utility. A credible utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for use. In contrast to general utility, a specific utility will be specific to the claimed subject matter. A substantial utility defines a real world utility of the invention and utilities that require or constitute carrying out further research to identify or reasonably confirm a real world context use are not substantial utility (see utility guidelines, in Federal Register January 5, 2001, Volume 66, Number 5, Pages 1092-1099).

The claims of the instant invention are drawn to a polypeptide of SEQ ID NO:1, or a polypeptide of SEQ ID NO:1, wherein one or several amino acids are deleted, substituted or added, DNA of SEQ ID NO:2 which encodes the polypeptide of SEQ ID NO:1 or a polypeptide of SEQ ID NO:1, wherein one or several amino acids are deleted, substituted or added, molecules which hybridize to SEQ ID NO:2, vectors, transformants or recombinant cells, a method for expressing the protein in a recombinant host cells and an agent for reducing the side effects of chemotherapy comprising a polypeptide of SEQ ID NO:1, or a polypeptide of SEQ ID NO:1, wherein

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one or several amino acids are deleted, substituted or added. The protein disclosed as SEQ ID NO:1 is designated in the specification as a transporter polypeptide which transports nucleoside molecules into cells or "discharges them from cells" (page 5, 2<sup>nd</sup> paragraph). To analyze the utility of the claimed invention one must determine if the polypeptide of SEQ ID NO:1 (or said polypeptide wherein one or several amino acids are deleted, substituted or added), encoded by the polynucleotide of SEQ ID NO:2 has a well-established utility or a credible, specific and/or substantial asserted utility.

Applicants disclose that molecules encoding the nucleoside transporter were identified utilizing primers based on expressed sequence tag database (Example 1, page 70) and isolated from a human fetal kidney derived cDNA library (page 74, last paragraph). The polypeptide is identified as a human equilibrative nuclear transporter (hENT) by virtue of being 35% identical to known human nucleoside transporter (hENT1) and exhibiting 48% homology to the sequence of hENT1 when analogous amino acids are taken into consideration (page 77, 5<sup>th</sup> paragraph). Based on the structural similarity, the specification asserts that the newly disclosed polypeptide of SEQ ID NO:1 has similar biological activities.

Applicants teach that ENTs are involved in the physiological incorporation of nucleosides into mammalian cells (page 1, last paragraph). The nucleoside transport process is important in various physiological activities mediated by adenosine (page 2, 2<sup>nd</sup> paragraph) and that ENTs are pharmacological targets for such anti-platelet aggregation drugs as dipyridamole and dilazep (page 3, last paragraph). However, the instant application does not disclose a specific and substantial biological role for the specific polypeptide of SEQ ID NO:1, variants of said polypeptide, or nucleotides encoding said polypeptides.

The assertion that the disclosed polypeptide of SEQ ID NO:1 has biological activities similar to known hENT, based solely on structural similarity to a protein found in the sequence databases, cannot be accepted in the absence of supporting evidence.

The art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein

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structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, *Genome Research* 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, *Trends in Genetics* 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, *Nature Biotechnology* 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, *Trends in Genetics* 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then, most homologs must have different molecular and cellular functions. Finally, Bork et al. (1996, *Trends in Genetics* 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

Applicants assert that the DNA molecules of the instant invention can be used for the detection of mRNA in tissues and cells (page 60, 2<sup>nd</sup> paragraph). This is not a specific utility for DNA encoding the polypeptide of SEQ ID NO:1. Any isolated DNA or RNA molecule may be used to identify, isolate and detect hybridizing and/or binding partners.

While applicants teach a method of determining the nucleoside transporter activity of the polypeptide of the instant invention (page 46, section 4), the specification does not contain any working examples showing that the polypeptide of SEQ ID NO:1 actually exhibits nucleoside transporter activity. There are no working examples

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utilizing the polypeptides in the assay method taught in the specification. Applicants disclose that the polypeptide of the instant invention may be used to identify agonists or antagonists (page 47, section 5). However, this is not a substantial, real world utility for the instant invention because there is no disclosure of why one would wish to screen for agonists or antagonists of the disclosed polypeptide other than to further characterize the claimed invention itself, which does not constitute utility under 35 USC §101.

Applicants assert that the polypeptide of the instant invention may be used as “a preventive agent or a therapeutic agent for ischemic heart disease, cerebral disorder at the time of stroke, immune response accompanied by organ transplantation, malignant tumor, nephritis, pancreatitis or hypertension....Its applications as an analgesic, an antiplatelet agent, an agent for increasing activity of an antiviral agent or a malignant tumor treating agent and an agent for reducing side effects at the time of chemotherapy can also be expected” (page 63, last paragraph, bridging page 64, 1<sup>st</sup> paragraph). To establish the utility of the claimed polypeptide as a therapeutic agent, one must establish a nexus between the polypeptide of SEQ ID NO:1 and a specific disease process or condition. The specification has not asserted a specific and substantial utility for the claimed invention because the specification and/or the art fail to establish a connection between SEQ ID NO:1 structure, expression or activity or changes in structure, expression or activity and any specific disease state. Example 2 teaches Northern blot analysis of the mRNA encoding SEQ ID NO:1; the results in Figure 5 show a band corresponding to said mRNA observed in heart, brain, placenta, lung, liver, skeletal muscle, kidney and pancreas. However, by failing to provide any evidence or working examples of a connection between the polypeptide of SEQ ID NO:1 and a specific disease, or a connection between changes in expression of mRNA or the claimed polypeptide with any specific pathological condition, applicants fail to provide any guidance as to which disorders one would treat with the polypeptide of SEQ ID NO:1. Furthermore, King et al. (2006. Trends in Pharm Sci. 27:416-425) teach that while nucleoside analogues are currently used for the treatment of a limited number of diseases, to date no evidence directly links nucleoside transporters to disease pathogenesis (page 423, 2<sup>nd</sup> column, 2<sup>nd</sup> paragraph). Merely listing a large number of

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possibilities is not sufficient to identify or confirm a "real world" context of use; clearly, further research would be required to ascertain the function of SEQ ID NO:1, to identify a disease with which this polypeptide is associated, and provide motivation to identify agonists or antagonists of said polypeptide.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sup. CT, 1966). The court found that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

Therefore, based on the discussions above concerning the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the absence of teaching in the specification that the polypeptide of SEQ ID NO:1 functions as a nucleoside transporter, and the failure to teach a nexus between the polypeptide of SEQ ID NO:1 and any disease or pathological condition, the specification fails to teach the skilled artisan a function for the polypeptide of SEQ ID NO:1 encoded by the DNA of SEQ ID NO:2. Since the polypeptide of SEQ ID NO:1, or its encoding nucleic acid molecule (SEQ ID NO:2) are not supported by a specific and substantial utility, or a well-established utility, then expression vectors, and transformants comprising the nucleic acids also do not possess utility.

Claims 1-12, 29, 42 and 46-48 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Furthermore, in addition to the issues raised in the utility rejection, claims 2, 5-12, 29, 42, 46-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, even if it were enabled for a polypeptide of SEQ ID NO:1 encoded by a nucleic acid of SEQ ID NO:2 would not be found to reasonably provide enablement for a polypeptide which comprises an amino acid sequence of SEQ ID NO:1 wherein one or several amino acids are deleted, substituted or added, a nucleotide sequence encoding said amino acid sequence, or a DNA sequence which hybridizes to said nucleotide sequence. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. If the utility rejection was to be withdrawn, these rejections would remain.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability, 5) existence of working samples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are broadly drawn to polypeptides comprising SEQ ID NO:1 which one or several amino acids deleted, substituted or added, DNA encoding said polypeptides, DNA which hybridizes with DNA encoding said polypeptides, plasmids, vectors, transformants (host cells), a method of producing said polypeptides, and a therapeutic agent comprising said polypeptides. The claims encompass variant polypeptides encoded by variant nucleic acids. These claims are overly broad since insufficient guidance is provided as to which of the myriad polypeptides will retain the activity of nucleoside transport and which of the variant nucleic acids would encode polypeptides which will retain recited activities. While the claims are directed to variant polypeptides encoded by variant nucleic acids, Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible variant polypeptides.

Variants of SEQ ID NOs:1 and 2 are not enabled for the following reasons. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and activity sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, *Biochemistry* 29:8509-8517; Ngo et al., 1994, *The Protein Folding Problem and Tertiary Structure Prediction*, pp. 492-495). However, applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein

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structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 7, 11 and 48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The invention appears to employ novel biological materials, specifically plasmids (plasmid p46-1). Since the biological materials are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. If the biological materials are not so obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the biological materials. The specification does not disclose a repeatable process to obtain the biological materials and it is not apparent if the biological materials are readily available to the public. It is noted that Applicants have deposited the biological materials (page 21 of the specification), but there is no indication in the specification as to public availability. If the deposit is made under the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific biological materials have been deposited under the Budapest Treaty and that the biological materials will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, and that the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer, would satisfy the deposit requirement made herein. If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. §§ 1.801-1.809, Applicants may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of deposit will be made (see 37 C.F.R. § 1.807); and

(e) the deposit will be replaced if it should ever become inviable.

Applicants' attention is directed to M.P.E.P. §2400 in general, and specifically to §2411.05, as well as to 37 C.F.R. § 1.809(d), wherein it is set forth that "the specification shall contain the accession number for the deposit, the date of the deposit, the name and address of the depository, and a description of the deposited material sufficient to specifically identify it and to permit examination." The specification should be amended to include this information; however, Applicants are cautioned to avoid the entry of new matter into the specification by adding any other information.

Claims 2, 5-12, 29, 42, 46-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim (s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polypeptide variants of SEQ ID NO:1 wherein one or several amino acids are deleted, substituted or added and nucleic acids encoding said variants. The claims do not require that the polypeptide possess any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides encoded by a genus of nucleotides that is defined only by a reference sequence, hybridization ability or the biological activity of nucleoside transport.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of a reference sequence or hybridization ability. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide written description of the claimed genus.

*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides or nucleic acids, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO:1, encoded by a DNA of SEQ ID NO:2, but not the full breadth of the

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claims meet the written description provision of 35 U.S.C. 112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

**35 U.S.C. § 112, Second Paragraph**

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 5-12, 29, 42, 46-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is vague and indefinite in reciting "a polypeptide which comprises .....the amino acid sequence described in SEQ ID NO:1....wherein one or several amino acids are deleted, substituted or added.....". Applicants have not provided any upper limit to the number of amino acids encompassed by the term "several". Therefore, the metes and bounds of the claimed invention cannot be determined.

Claims 5-12, 29, 42, and 46-48 are included in this rejection as dependent upon Claim 2.

Claim 5 is vague and indefinite in reciting "A DNA which hybridizes with the DNA .....under stringent conditions.....". "Stringent conditions" may refer to low, medium or high stringency conditions. Claims which recited stringent conditions are indefinite because there is no limiting definition of such in the specification and the metes and bounds of that which will hybridize are dependent upon the conditions under which the hybridization is performed. The specification (page 7, last paragraph bridging page 8, 3<sup>rd</sup> paragraph) recites "DNA which hybridizes under stringent conditions.....means a DNA which is obtained by the colony hybridization method, the plaque hybridization method, the Southern blot hybridization method or the like....." and goes on to recite illustrative examples. The definition in the specification is not limiting; thus, the metes and bounds of the claim cannot be determined.

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Claim 47 is included in this rejection as dependent upon claim 5

Claims 8, 9 and 48 are vague and indefinite in reciting "A transformant" or "the transformant". It is unclear if applicants' intend the transformants used in culture to produce a recombinant protein (as disclosed in the specification on page 33, section 2 bridging section 3, page 39) or a transformant used *in vivo* for <sup>or as a result of</sup> gene therapy (as disclosed in the specification on page 32, last paragraph). This rejection could be overcome by amending the claims to recite, for example, "An isolated transformant...." because such an amendment would clarify that the claims are directed to transformant made and used in culture.

### 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 2, 5, 6, 8, 9, 42, 46, and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Griffiths et al (1997. Nature Med. 3:89-93, cited on IDS of 10 May 2001, reference 1). The claims of the instant invention are drawn to a polypeptide of SEQ ID NO:1 wherein one or several amino acids are deleted, substituted or added, DNA encoding said polypeptides, vectors and transformants. Griffiths et al. teach a human nucleoside transporter with 28.1% sequence identity to SEQ ID NO:1 (best local similarity, 33.6%) (page 90, Figure 1), thus anticipating limitations of claim 2. The reference teaches cDNA encoding said polypeptide, construction of plasmid DNA and

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transfection of *Xenopus* oocytes (page 92, 2<sup>nd</sup> column, last paragraph), thus anticipating limitations of claims 6, 8, 9, 42, 46 and 47. The reference teaches primers which hybridize with DNA encoding the human nucleoside transporter (page 92, 1<sup>st</sup> column, 2<sup>nd</sup> paragraph), thus anticipating the limitations of claim 5. Therefore, the teachings of Griffiths et al. anticipate all the limitations of Claims 2, 5, 6, 8, 9, 42, 46, and 47.

***Art made of record:***

The following art is made of record and not relied upon is considered pertinent to applicant's disclosure. Donoho et al. (USPGPUB 2002/0082405, priority claimed to provisional 60/187,120, filed 6 March 2000) disclose an amino acid sequence (SEQ ID NO:38) that is 100% identical to SEQ ID NO:1 of the claimed invention. The reference teaches that the amino acid is a nucleoside transporter. Donoho et al. also teach nucleic acids encoding said amino acid sequence, nucleic acids hybridizing to coding sequences, vectors, transformants and methods of producing the protein. However, the provisional application was filed after applicants' priority date of 26 August 1999.

***Conclusion:***

No claims are allowed.

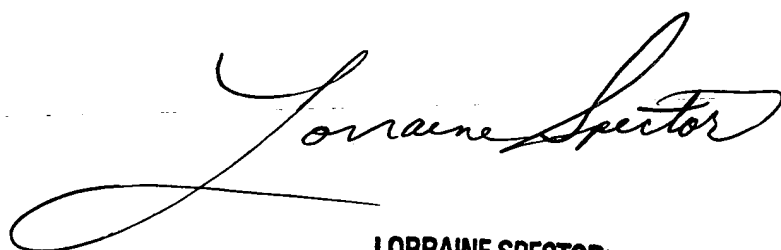
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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shulamith H. Shafer, Ph.D. whose telephone number is 571-272-3332. The examiner can normally be reached on Monday through Friday, 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SHS

A handwritten signature in cursive script that reads "Lorraine Spector". The signature is written in black ink and is positioned above the printed name and title.

**LORRAINE SPECTOR  
PRIMARY EXAMINER**